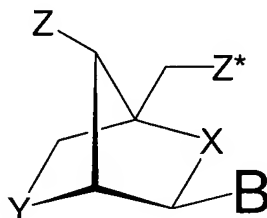


AMENDMENTS TO THE CLAIMS

1. (Canceled)
2. (Currently Amended) A compound of claim 91, which modulates the expression of thioredoxin.
3. (Canceled)
4. (Currently Amended) The compound according to claim 91, which is an antisense oligonucleotide.
5. (Currently Amended) The compound according to claim 91, comprising at least one nucleotide analogue.
6. (Currently Amended) The compound according to claim 91, comprising at least one Locked Nucleic Acid (LNA) unit.
7. (Previously Presented) The compound according to claim 6, wherein the Locked Nucleic Acid (LNA) unit has the structure of the general formula



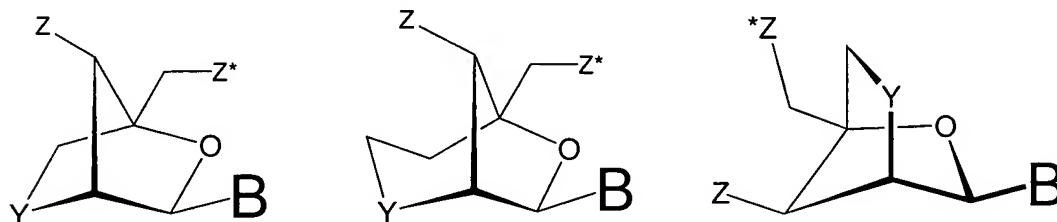
X and Y are independently selected among the groups -O-, -S-, -N(H)-, N(R)-, -CH<sub>2</sub>- or -CH- (if part of a double bond), -CH<sub>2</sub>-O-, -CH<sub>2</sub>-S-, -CH<sub>2</sub>-N(H)-, -CH<sub>2</sub>-N(R)-, -CH<sub>2</sub>-CH<sub>2</sub>- or -CH<sub>2</sub>-CH- (if part of a double bond), -CH=CH-, where R is selected from hydrogen and C<sub>1-4</sub>-alkyl ;

Z and Z\* are independently absent, selected among an internucleoside linkage, a terminal group or a protecting group;

B constitutes a natural or non-natural nucleobase;

and the asymmetric groups may be found in either orientation.

8. (Original) The compound according to claim 6 or 7, wherein at least one nucleotide comprises a Locked Nucleic Acid (LNA) unit according any of the formulas



wherein Y is independently selected from -O-, -S-, -NH-, and N(R<sup>H</sup>);

Z and Z\* are independently absent, selected among an internucleoside linkage, a terminal group or a protecting group; and

B constitutes a natural or non-natural nucleobase.

9. (Currently Amended) The compound according to claim 91, wherein the nucleotide analogue comprises an internucleoside linkage selected from the group consisting of -O-P(O)<sub>2</sub>-O-, -O-P(O,S)-O-, -O-P(S)<sub>2</sub>-O-, -S-P(O)<sub>2</sub>-O-, -S-P(O,S)-O-, -S-P(S)<sub>2</sub>-O-, -O-P(O)<sub>2</sub>-S-, -O-P(O,S)-S-, -S-P(O)<sub>2</sub>-S-, -O-PO(R<sup>H</sup>)-O-, O-PO(OCH<sub>3</sub>)-O-, -O-PO(NR<sup>H</sup>)-O-, -O-PO(OCH<sub>2</sub>CH<sub>2</sub>S-R)-O-, -O-PO(BH<sub>3</sub>)-O-, -O-PO(NHR<sup>H</sup>)-O-, -O-P(O)<sub>2</sub>-NR<sup>H</sup>-, -NR<sup>H</sup>-P(O)<sub>2</sub>-O-, -NR<sup>H</sup>-CO-O-, where R<sup>H</sup> is selected from hydrogen and C<sub>1-4</sub>-alkyl.

10. – 13. (Canceled)

14. (Currently Amended) The compound according to claim 413, wherein the antisense oligonucleotide is a gapmer.

15. (Currently Amended) The compound according to claim 91, wherein the antisense oligonucleotide is a 13, 14, 15, 16, 17, 18, 19, 20 or 21-mer in length.

16. (Currently Amended) The compound according to claim 91, comprising at least 2 LNA units, such as 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or 21 LNA units.

17. – 46. (Cancelled)

47. (Currently Amended) A conjugate comprising the compound according to claim 1 and at least one non-nucleotide or non-polynucleotide moiety covalently attached to said compound.

48. (Currently Amended) A pharmaceutical composition comprising a compound as defined in claim Currently Amended 91 or a conjugate as defined in claim 47; and a pharmaceutically acceptable diluent, carrier or adjuvant.

49. (Previously Presented) The pharmaceutical composition according to claim 48, further comprising at least one chemotherapeutic agent.

50. (Previously Presented) The pharmaceutical composition according to claim 49, wherein said chemotherapeutic compound is selected from the group consisting of adrenocorticosteroids, such as prednisone, dexamethasone or decadron; altretamine (hexalen, hexamethylmelamine (HMM)); amifostine (ethyol); aminoglutethimide (cytadren); amsacrine (M-AMSA); anastrozole (arimidex); androgens, such as testosterone; asparaginase (elspar); bacillus calmette-gurin; bicalutamide (casodex); bleomycin (blenoxane); busulfan (myleran); carboplatin (paraplatin); carmustine (BCNU, BiCNU); chlorambucil (leukeran); chlorodeoxyadenosine (2-CDA, cladribine, leustatin); cisplatin (platinol); cytosine arabinoside (cytarabine); dacarbazine (DTIC); dactinomycin (actinomycin-D, cosmegen); daunorubicin (cerubidine); docetaxel (taxotere); doxorubicin (adriamycin); epirubicin; estramustine (emcyt); estrogens, such as diethylstilbestrol (DES); etoposide (VP-16, VePesid, etopophos); fludarabine (fludara); flutamide (eulexin); 5-FUDR (floxuridine); 5-fluorouracil (5-FU); gemcitabine (gemzar); goserelin (zodalex); herceptin (trastuzumab); hydroxyurea (hydrea); idarubicin (idamycin); ifosfamide; IL-2 (proleukin, aldesleukin); interferon alpha (intron A, roferon A); irinotecan (camptosar); leuprolide (lupron); levamisole (ergamisole); lomustine (CCNU); mechlorathamine (mustargen, nitrogen mustard); melphalan (alkeran); mercaptopurine (purinethol, 6-MP); methotrexate (mexate); mitomycin-C (mutamucin); mitoxantrone (novantrone); octreotide (sandostatin); pentostatin (2-deoxycoformycin, nipent); plicamycin (mithramycin, mithracin); prorocarbazine (matulane); streptozocin; tamoxifen (nolvadex); taxol (paclitaxel); teniposide (vumon, VM-26); thiotepa;

topotecan (hycamtin); tretinoin (vesanoid, all-trans retinoic acid); vinblastine (valban); vincristine (oncovin) and vinorelbine (navelbine).

51. (Currently Amended) A pharmaceutical composition comprising the compound of claim 91, which further comprises a pharmaceutically acceptable carrier.

52. (Currently Amended) A pharmaceutical composition comprising the compound of claim 91, which is employed in a pharmaceutically acceptable salt.

53. (Currently Amended) A pharmaceutical composition comprising the compound of claim 91, which is constitutes a pro-drug.

54. (Currently Amended) A pharmaceutical composition comprising the compound of claim 91, which further comprises an antiinflammatory compounds and/or antiviral compounds.

55. – 63. (Canceled)

64. (Withdrawn, Currently Amended) A method for treating cancer, said method comprising administering a compound as defined in claim 91, a conjugate as defined in claim 51 or a pharmaceutical composition as defined in claim 48 to a patient in need thereof.

65. (Withdrawn) The method according to claim 64, wherein said cancer is in the form of a solid tumor.

66. (Withdrawn) The method according to claim 64, wherein said cancer is a carcinoma.

67. (Withdrawn) The method according to claim 66, wherein said carcinoma is selected from the group consisting of malignant melanoma, basal cell carcinoma, ovarian carcinoma, breast carcinoma, non-small cell lung cancer, renal cell carcinoma, bladder carcinoma, recurrent superficial bladder cancer, stomach carcinoma, prostatic carcinoma, pancreatic carcinoma, lung

carcinoma, cervical carcinoma, cervical dysplasia, laryngeal papillomatosis, colon carcinoma, colorectal carcinoma and carcinoid tumors.

68. (Withdrawn) The method according to claim 67, wherein said carcinoma is selected from the group consisting of malignant melanoma, non-small cell lung cancer, breast carcinoma, colon carcinoma and renal cell carcinoma.

69. (Withdrawn) The method according to claim 68, wherein said malignant melanoma is selected from the group consisting of superficial spreading melanoma, nodular melanoma, lentigo maligna melanoma, acral melanoma, amelanotic melanoma and desmoplastic melanoma.

70. (Withdrawn) The method according to claim 64, wherein said cancer is a sarcoma.

71. (Withdrawn) The method according to claim 70, wherein said sarcoma is selected from the group consisting of osteosarcoma, Ewing's sarcoma, chondrosarcoma, malignant fibrous histiocytoma, fibrosarcoma, arteriosclerosis, psoriasis, diabetic retinopathy, rheumatoid arthritis, asthma, warts, allergic dermatitis and Kaposi's sarcoma.

72. (Withdrawn) The method according to claim 64, wherein said cancer is a glioma.

73. (Withdrawn) A method of inhibiting the expression of TRX, in cells or tissues comprising contacting said cells or tissues with the compound according to claim 1 so that expression of TRX is inhibited.

74. (Withdrawn, Currently Amended) A method of modulating expression of a gene involved in a cancer disease comprising contacting the gene or RNA from the gene with an oligomeric compound as set forth in claim 91, ~~wherein said compound has a sequence comprising at least an 8 nucleobase portion of SEQ ID NO: 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56 or 57~~ whereby gene expression is modulated.

75. (Canceled)

76. (Withdrawn) The method of claim 74, wherein the compound hybridizes with messenger RNA of the gene to inhibit expression thereof.

77. (Withdrawn, Currently Amended) A method of treating a mammal suffering from or susceptible from a cancer disease, comprising:  
administering to the mammal an therapeutically effective amount of a compound as set forth in claim 1~~an oligonucleotide targeted to TRX that comprises one or more LNA units.~~

78. (Withdrawn) The method according to claim 74, wherein the cancer disease is a lung, breast, colon, prostate, pancreas, lung, liver, thyroid, kidney, brain, testes, stomach, intestine, bowel, spinal cord, sinuses, bladder, urinary tract or ovaries cancer.

79. (Withdrawn, Currently Amended) A method of modulating the red blood cell proliferation, cellular proliferation, ion metabolism, glucose and energy metabolism, pH regulation or matrix metabolism comprising contacting a cell with the antisense compound of claim 91 so that the cell is modulated.

80. (Withdrawn, Currently Amended) A method of inhibiting the proliferation of cells comprising contacting cells in vitro with an effective amount of the antisense compound of claim 91, so that proliferation of the cells is inhibited.

81. (Currently Amended) The method of claim 80 wherein said cells are cancer cells.

82. (Withdrawn, Currently Amended) A method of inhibiting the expression of TRX in human cells or tissues comprising contacting human cells or tissues with the compound of claim 91 so that expression of TRX is inhibited.

83. (Withdrawn, Currently Amended) A method of treating an animal having a disease or condition associated with TRX comprising administering to an animal having a disease or condition associated with TRX a therapeutically or prophylactically effective amount of the antisense compound of claim 91 so that expression of TRX is inhibited.

84. (Withdrawn) The method of claim 83 wherein the disease or condition is a hyperproliferative condition.

85. (Withdrawn) The method of claim 84 wherein the hyperproliferative condition is cancer.

86. (Withdrawn, Currently Amended) A method of treating a human having a disease or condition characterized by a reduction in apoptosis comprising administering to a human having a disease or condition characterized by a reduction in apoptosis a prophylactically or therapeutically effective amount of the antisense compound of claim 91.

87. (Withdrawn, Currently Amended) A method of modulating apoptosis in a cell comprising contacting a cell with the antisense compound of claim 91 so that apoptosis is modulated.

88. (Withdrawn, Currently Amended) A method of modulating cytokinesis in a cell comprising contacting a cell with the antisense compound of claim 91 so that cytokinesis is modulated.

89. (Withdrawn, Currently Amended) A method of modulating the cell cycle in a cell comprising contacting a cell with the antisense compound of claim 91 so that the cell cycle is modulated.

90. (Withdrawn, Currently Amended) A method of inhibiting the proliferation of cells comprising contacting cells with an effective amount of the antisense compound claim 91, so that proliferation of the cells is inhibited.

91. (New) A compound consisting of 12-50 nucleotides and/or nucleotide analogues, wherein said compound comprises a subsequence of at least 8 nucleotides or nucleotide analogues, said

subsequence being located within the sequence caaggaatatcacgtt and wherein at least one of said nucleotides in said sequence has been replaced by a corresponding nucleotide analogue.

92. (New) The compound of claim 91, wherein said corresponding nucleotide is selected from the group consisting of LNA sugar, 2'-O-methyl RNA sugar, 2'-fluoro DNA sugar, 2'-MOE RNA sugar, 2'-O-(3-amino)propyl RNA sugar and 2'-O-(3-hydroxy)propyl RNA sugar.

93. (New) The compound of claim 92, wherein said corresponding nucleotide is LNA.

94. (New) The compound of claim 93, wherein said LNA is selected from the group consisting of thio-LNA, amino-LNA and oxy-LNA.

95. (New) The compound of claim 94, wherein said LNA is beta-D-oxy-LNA.

96. (New) The compound of claim 91, wherein said compound comprises a subsequence of at least 12 nucleotides or nucleotide analogous.

97. (New) The compound of claim 91, wherein said compound consists of 12-20 nucleotides and/or nucleotide analogues.

98. (New) The compound of claim 91, wherein said compound comprises the sequence CAAGgaatatcaCGTT or CAAGgaatatcaCGTt, wherein uppercase letters denote a beta-D-oxy-LNA and lowercase letters denote a DNA sugar, and wherein said nucleotides and/or nucleotide analogues are linked together by a phosphate group, a phosphorothioate group, or a combination thereof.

99. (New) The compound of claim 98, wherein said compound comprises the sequence C<sub>5</sub>A<sub>5</sub>A<sub>5</sub>G<sub>5</sub>g<sub>5</sub>s<sub>5</sub>a<sub>5</sub>s<sub>5</sub>t<sub>5</sub>s<sub>5</sub>a<sub>5</sub>t<sub>5</sub>s<sub>5</sub>c<sub>5</sub>s<sub>5</sub>A<sub>5</sub>C<sub>5</sub>G<sub>5</sub>T<sub>5</sub>T, wherein uppercase letters denote a beta-D-oxy-LNA and lowercase letters denote a DNA sugar, and wherein the subscript "s" denotes a phosphorothioate linkage.



100. (New) The compound of claim 98, wherein said compound consists of the sequence  $C_sA_sA_sG_sG_sA_sA_sT_sA_sT_sC_sA_sC_sG_sT_sT$ , wherein uppercase letters denote a beta-D-oxy-LNA and lowercase letters denote a DNA sugar, and wherein the subscript "s" denotes a phosphorothioate linkage.

101. (New) The compound of claim 98, wherein said compound comprises the sequence  $C_oA_oA_oG_oG_sA_sA_sT_sA_sT_sC_sA_sC_oG_oT_oT$ , wherein uppercase letters denote a beta-D-oxy-LNA and lowercase letters denote a DNA sugar, and wherein the subscript "s" denotes a phosphorothioate linkage and the subscript "o" denotes a phosphate linkage.

102. (New) The compound of claim 98, wherein said compound consists of the sequence  $C_oA_oA_oG_oG_sA_sA_sT_sA_sT_sC_sA_sC_oG_oT_oT$ , wherein uppercase letters denote a beta-D-oxy-LNA and lowercase letters denote a DNA sugar, and wherein the subscript "s" denotes a phosphorothioate linkage and the subscript "o" denotes a phosphate linkage.

103. (New) The compound of claim 98, wherein said compound comprises the sequence  $C_sA_sA_sG_sG_sA_sA_sT_sA_sT_sC_sA_sC_sG_sT_sT$ , wherein uppercase letters denote a beta-D-oxy-LNA and lowercase letters denote a DNA sugar, and wherein the subscript "s" denotes a phosphorothioate linkage.

104. (New) The compound of claim 98, wherein said compound consists of the sequence  $C_sA_sA_sG_sG_sA_sA_sT_sA_sT_sC_sA_sC_sG_sT_sT$ , wherein uppercase letters denote a beta-D-oxy-LNA and lowercase letters denote a DNA sugar, and wherein the subscript "s" denotes a phosphorothioate linkage.

105. (New) The compound of any of claims 91-104, wherein LNA cytosine (C) is LNA 5' methyl cytosine (5-MeC).